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ABSTRACT

Averaged evoked potential (AEP) is an event-related brain response obtained by averaging the scalp electrical potentials elicited by repeated presentations of the same event. It has proven to be an accurate measure of the activity of the mature human brain when involved in a wide variety of psychological tasks. Distinct psychological processes appear to be associated with changes in the averaged evoked potential at different points in time with respect to the stimulus event. When an infrequent or unexpected stimulus is presented to the adult, a characteristic enhancement of the late positive component (LPC) of the averaged evoked cortical potential is observed. To test whether this effect obtains near birth, in two studies, low and high-probability visual stimuli were presented to twenty-nine 3-month-old infants. Electrical potentials were recorded from occipital and parietal scalp sites. A clear LPC effect was observed at both sites between 300-600 msec following the onset of the infrequent stimulus. This is the first demonstration of an LPC effect in infants, reflecting cognitive processing involving memory. A method for analyzing single trials is incorporated, demonstrating individual differences in early cognitive functioning. (Author/RH)

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Evidence of Visual Memory in the Cortical Evoked Potential of Human Infants[1]

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Abstract

When an infrequent or unexpected stimulus is presented to the adult, a characteristic enhancement of the late positive component (LPC) of the averaged evoked cortical potential is observed. To test whether this effect obtains near birth, we presented low and high probability visual stimuli to 3-month-old infants. Electrical potentials were recorded from occipital and parietal scalp sites (O_z and O_{pz}). A clear LPC effect was observed at both sites between 300-600 msec following the onset of the infrequent stimulus. This is the first demonstration of an LPC effect in infants, reflecting cognitive processing involving memory. A method for analyzing single trials is incorporated, demonstrating individual differences in early cognitive functioning.

The averaged evoked potential (AEP) is an event-related brain response obtained by averaging the scalp electrical potentials elicited by repeated presentations of the same event. It has proven to be an accurate measure of the activity of the mature human brain when involved in a wide variety of psychological tasks (Regan, 1972). Complex mental processing involving memory, attention, and categorization, as well as sensory discrimination, can be indexed by changes in the evoked potential (Desmedt, 1977; Thatcher & John, 1977; John & Schwartz, 1978).

Distinct psychological processes appear to be associated with changes in the AEP at different points in time with respect to the stimulus event. Thus, in the first 300 msec, the cortical evoked potential mirrors sensory detection of simple stimulus features such as brightness, color, and contour. Changes in the AEP following the sensory components, from 300 msec onward, typically index more cognitive operations.

An enhancement of the late positive component (LPC, P_3 or P_{300}) has been shown to occur in adults when they are engaged in tasks involving selective attention, stimulus novelty and uncertainty, and match-mismatch operations (Sutton, Bearen, Zubin & John, 1965; Thatcher, 1977; Courchesne, Hillyard & Galanbos, 1975). There have been many recent demonstrations that the AEP is

related to sensory processing in human infants as it is in adults (Atkinson, Braddick & Braddick, 1974; Harter & Suitt, 1970; Marg, Freeman, Peltzman & Goldstein, 1976; Sokol & Dobson, 1976). However, although young infants have provided ample evidence of stimulus encoding in behavioral studies of memory and habituation (Cohen & Gelber, 1975; Fantz, Fagan & Miranda, 1975), LPC effects in infants have received little attention by researchers. We report in this paper the first demonstration of positive evidence for the LPC effect in normal 3-month olds. We also report data collected from a group of atypical infants, Down's Syndrome infants, tested with the same procedure.

We chose a paradigm that would maximize the infant's attention and develop an expectancy for a stimulus event while remaining comparable to adult LPC paradigms. This paradigm was a variant of the design originally employed by Sutton et al. (1965) to establish stimulus expectancies. Sutton et al. verbally instructed subjects to look for novel events in a stimulus sequence. The LPC effect occurred in response to these novel events. Since we could not verbally instruct infants to look for the low probability stimulus, we first presented trials of the high probability stimulus alone, developing a strong stimulus expectancy. After this familiarization phase, we randomly added the low probability stimulus. Since the magnitude of the LPC effect is inversely related to the probability of the stimulus occurrence in this situation, we felt that this would maximize the chances of eliciting an LPC effect in infants.

Each infant saw two simple stimuli during the course of the experiment. The stimuli were two square wave gratings with frequencies of .4 cy/deg and 1.0 cy/deg.

Each was 30° x 30° with a luminance of 1.45 log ftL and a mean contrast of 75%. These stimuli were chosen because infants of this age are sensitive to variations in spatial frequency.

For a given infant, one or the other of the square wave gratings was initially presented a minimum of 40 consecutive times during a familiarization phase (100% probability of occurrence). A test phase followed in order to assess whether a novel event would result in an LPC effect. During this test phase, the familiarized grating continued to occur with a high probability (80%) while the second grating was randomly introduced into the stimulus sequence with a low probability of occurrence (20%), with the restriction that this stimulus never occurred twice in succession. A minimum of 120 trials was included in this test phase. Following the completion of this test phase, all infants received a second familiarization phase and a second test phase, identical to the first, but with the first and second gratings exchanged.

Babies viewed the stimuli on a large screen while seated on a parent's lap. Each stimulus was presented for 500 msec with an interstimulus interval of 500 msec. EEG was recorded from monopolar leads O_z and O_{pz} (located half the distance between O_z and P_z) referenced to the left mastoid. EOG potentials were recorded from two transverse eye leads. The signals were stored on FM tape. Averaged evoked potentials were computed offline on a PDP-12 computer (sampling rate was one point per 3 msec, with an epoch length of 600 msec). Individual records were edited offline for eye and/or head movement artifacts.

Thirteen normal, term 3-month-old infants ($\bar{X}$ = 94 days; range 87-103 days) provided sufficient data in all phases of the experiment. After editing, those

infants who gave 32 artifact-free low probability trials were included in the study. For all comparisons, an equal number of artifact-free trials were included in the AEP for each subject. In Figure 1 the infant data are plotted. One curve was obtained by averaging EPs from both familiarization phases (100%). Likewise, the other curve represents the average of EPs obtained for the 20% stimuli presented during the two test phases. To allow a comparison of late potentials, the two curves are superimposed with respect to the mean voltage in the first 30 msec following stimulus onset (initial baseline referent). Inspection of the EPs suggested a late-positive enhancement in the low probability condition (20%) for most of the infants. Areas under the EP curve from 300-600 msec were computed for O_z with respect to initial baseline referent for each infant for the 100% condition (the two 100% phases combined) and the 20% condition (the two 20% phases combined). A difference score (20% minus 100%) was calculated in order to assess late potential effects. The upper portion of Figure 2 provides the distribution of area difference scores for all infants for this comparison. Area difference scores were significantly greater than zero (Wilcoxon matched-pairs, signed ranks test, $T = 15$, $N = 13$, $p < .025$) indicating an LPC effect. To insure that the foregoing differences were not due to chance fluctuations in late potentials, we calculated area difference scores for the two high probability conditions (80% minus 100%) where a strong LPC was not expected. As can be seen in the lower portion of Figure 3 the distribution of area difference scores for the 80% minus 100% comparison did not differ significantly from zero (Wilcoxon $T = 50.5$, $N = 13$, n.s.),with no evidence of the positive skew seen in the 20% minus 100% comparison.

The initial baseline referent against which we chose to measure the LPC is one that is commonly used since early potentials are not highly correlated with later components of the EP. However, to insure that the LPC effect was not the result of systematic variation in this baseline, other components, N_1 and the mean of N_1 and P_2, of the EP were also used as baselines against which to assess late potentials. A similar pattern of results emerged. Positive area difference scores were significantly greater than zero for the 20% minus 100% comparison both when N_1 was used as baseline (Wilcoxon T = 12, N = 13, $p < .01$) and when the mean value of N_1 and P_2 components was used as baseline (Wilcoxon T = 7, N = 13, $p < .005$). As was the case with the initial baseline referent, this was not true for the 80% minus 100% comparison (N_1 referent: Wilcoxon T = 44, N = 13, n.s.; mean N_1-P_2 referent: Wilcoxon T = 39, N = 13, n.s.). Thus, all baseline referents provided equally strong evidence of an LPC effect.

We next examined whether our experimental condition had affected the magnitudes of early sensory components (first 300 msec) of the EP. No significant positive departure from zero was found in the area difference scores for the 20% minus 100% comparison, nor for the 80% minus 100% comparison, regardless of the baseline referent chosen. Thus, it appears the early components of the EP were not strongly implicated in the LPC effects observed.

In the adult the LPC for a given task is often restricted to a narrow interval beyond 300 msec. However, the observed LPC effect in this study was not found to be restricted to any particular time interval, at least from 300 up to 600 msec, the end point of analysis in this study. Area difference scores were significantly greater than zero with respect to initial baseline referent between 300-450 msec (Wilcoxon T = 14, N = 13, $p < .01$), 350-500 msec (Wilcoxon T = 17, N = 13, $p < .025$), and 450-600 msec (Wilcoxon T = 15, N = 13, $p < .01$). Further,

area difference scores for individual infants were highly correlated across intervals. A very high and significant correlation was found between area difference scores from the 300-450 msec and 450-600 msec intervals for the initial baseline referent comparison (Spearman rank correlation coefficient, $R_s = +0.94$, $N = 13$, $p < .01$). Thus, if an infant exhibited an LPC effect, he tended to do so across the entire 300-600 msec interval. Effects similar to the foregoing were obtained for the other two referents, N_1 and mean N_1-P_2.

The observed LPC effect was also not restricted to a single scalp electrode. Recordings from O_{pz} revealed a pattern of results which closely resembled those from O_z. Area difference scores are shown in Figure 2 for O_{pz}. Area difference scores across 300-600 msec were significantly greater than zero for the 20% minus 100% comparison when the initial baseline referent was used (Wilcoxon $T = 16$, $N = 13$, $p < .025$). However, the LPC effect at O_{pz} was significant for all three baseline measures only beyond 450 msec, suggesting a later appearance at O_{pz} than at O_z.

We next report data collected from 12 Down's Syndrome infants ranging in age from 3 to 15 months (median = 8 months) under the same experimental procedure. We wish to note that even though membership in this group is based on the diagnosis of Down's Syndrome, this does not suggest that this sample is homogeneous in behavioral capacity and brain functioning. Area difference scores for O_z were significantly different from zero for the 20% minus 100% comparison when the initial baseline referent was used (Wilcoxon $T = 16$, $N = 12$, $p < .05$). When the interval 300-600 msec was divided into three smaller intervals the effect appeared only in the later 450-600 msec interval (300-450 msec interval: Wilcoxon $T = 22$, $N = 12$, n.s.; 350-500 msec interval: Wilcoxon $T = 21$, $N = 12$,

n.s.; 450-600 msec interval: Wilcoxon T = 17, N = 12, $p < .05$). When other referents were used to assess the LPC effect there were no significant differences from zero (N1 referent: 300-450 msec interval Wilcoxon T = 36, N = 12, n.s.; 350-500 msec interval Wilcoxon T = 33, N = 12, n.s.; 450-600 msec interval Wilcoxon T = 41, N = 12, n.s.; mean N1-P2 referent: 300-450 msec interval Wilcoxon T = 25, N = 12, n.s.; 350-500 msec interval Wilcoxon T = 20, N = 12, n.s.; 450-600 msec interval Wilcoxon T = 26, N = 12, n.s.). The group of Down's infants gave very little evidence of a significant LPC effect, although they were, on the average, older than the normal infants.

Study 1 provides highly suggestive evidence that 3-month olds formed expectancies regarding the likelihood of occurrence of the events we presented. Evidence for these expectancies are LPC differences recorded from the scalp with similar temporal and polarity characteristics as the P_{300} in adults. A second study was conducted to confirm and extend our original results.

An additional 16 3-month olds were tested in Study 2 for the LPC effects. The .4 cy/deg grating used in the first study was again chosen as one of the stimuli. This slide, rotated 90^{o}, was also the second stimulus. Thus, the two stimuli were identical in their spatial frequency content, but differed in the orientation of the square wave grating (i.e., a vertical square wave grating and a horizontal square wave grating). These stimuli were chosen to rule out discrimination based solely on peripheral sensory fatigue, since

it is generally understood that processing of orientation is cortical (Doty, 1973).

The experimental conditions and procedures were identical to those of Study 1 and provided similar results. Area difference scores for the 20% minus 100% comparison were significantly greater than zero at O_z when initial baseline was used as referent, indicating a strong LPC effect (Wilcoxon T = 7, N = 14, $p < .005$). No significant difference was found for the 80% minus 100% comparison Wilcoxon T = 28, N = 14, n.s.). Similar results, indicating an LPC effect, were obtained from O_{pz} for the 20% minus 100% comparison using the initial baseline referent (Wilcoxon T = 20, N = 16, $p < .01$). Again, no significant difference was found for the 80% minus 100% comparison on the same measure (Wilcoxon T = 54, N = 16, n.s.). Finally, as in Study 1, no significant positive mean area difference was found among conditions for the first 300 msec or sensory portion of the EP.

It can be argued that the method of averaging evoked responses across a large number of trials obscures variations in the brain's response on individual trials. Averaging does not permit us to determine when the LPC effect occurs and how long it lasts within a session. We here report the use of the method of single trial analysis in young infants from Study 1 on single trials where we had a reason to believe the stimulus was at least detected.

We wanted to determine whether the LPC effect could be observed on single trials and to examine the consistency of the effect across trials. Therefore, each of the trials that contributed to an averaged response was examined. If the P2 component, indicative of detection, was clearly present on a given trial, that trial was included in the single trial analysis. This selection

was possible because the signal-to-noise ratio of the evoked response in human infants is much greater than in adults. An equal number of trials from the 20% and 100% conditions were included in the analysis. A linear discriminant function analysis was used to test the distinctiveness of the EP waveforms from the two conditions. Five predictor variables were used in the analysis. These were the mean EP voltages from: 1) 300-360 msec, 2) 360-420 msec, 3) 420-480 msec, 4) 480-540 msec, and 5) 540-600 msec, on each trial selected. For subjects showing a positive area difference score greater than 200 units (i.e., a likely LPC effect) (see Figure 2) the discriminant analysis correctly predicted single trials from the two conditions with 66% to 83% accuracy. In Figure 3 are plotted the AEPs for one infant in our study for the three conditions 100%, 80% and 20%. In this subject one can clearly detect an enhancement of the late positive component in the average evoked response in the 20% condition. In Figure 4 are plotted examples of correctly (hit) and incorrectly (miss) classified trials from the 100% condition for that infant. Note that on the single trials correctly predicted in the 100% condition there is no extended late positive component. In Figure 5 are plotted examples of correctly and incorrectly classified trials from the 20% condition for that same infant. Note that on the single trials correctly predicted in the 20% condition there is an enhancement of the late positive component as compared to misclassified trials. Thus, discriminant analysis was able to detect differences between the evoked responses of the two conditions, 100% and 20%, based on single trial data for this subject and other subjects showing a strong LPC effect.

A number of infants did not show a strong LPC effect as measured by averaging evoked responses. It is possible that some of these infants did not process the discrepancy between the stimuli. However, it is also possible that some infants did process the discrepancy on a limited number of trials, but not on other trials for reasons such as fatigue or inattention. We tested this hypothesis using the single trial method of analysis.

In Figure 6 are plotted the predictions for single trials from the 20% condition for a subject not showing a strong LPC effect. Trials 1-15 were selected in order from the first test phase and trials 16-27 from the second test phase. During the first test phase there is no indication of a distinction between low probability trials (20%) and high probability trials (100%). However, during the second test phase (trials 16-27) there is strong evidence that the low probability trials are distinct from the high probability trials, indicating the appearance of an LPC effect in this second test phase. Thus, in infants single trial analysis provides access to certain aspects of the LPC effect which could not be uncovered by averaging procedures.

We believe that the observed LPC indicates the development of expectancies on the part of the infant. The fact that no differences among conditions were observed for the early (0-300 msec) components of the EP strongly suggests that purely peripheral factors such as receptor or sensory fatigue were not totally responsible for the LPC effect. It should be noted that our stimuli were two very simple gratings varying only in spatial frequency or orientation and should not have required very elaborate processing. But, clearly, memory and discrimination were involved, since the LPC was only elicited by the

occurrence of an infrequent stimulus. Results from Study 2 also implicate cortical involvement in this process. The EP, with its efficiency relative to behavioral tests, may be an invaluable tool for the study of simple memory, attention and discrimination in both normal and abnormal pre-verbal infants. Finally, the addition of single trial analysis opens new avenues for further study of the temporal patterning of cognitive processing, and even reveals individual differences in the structure of early cognition.

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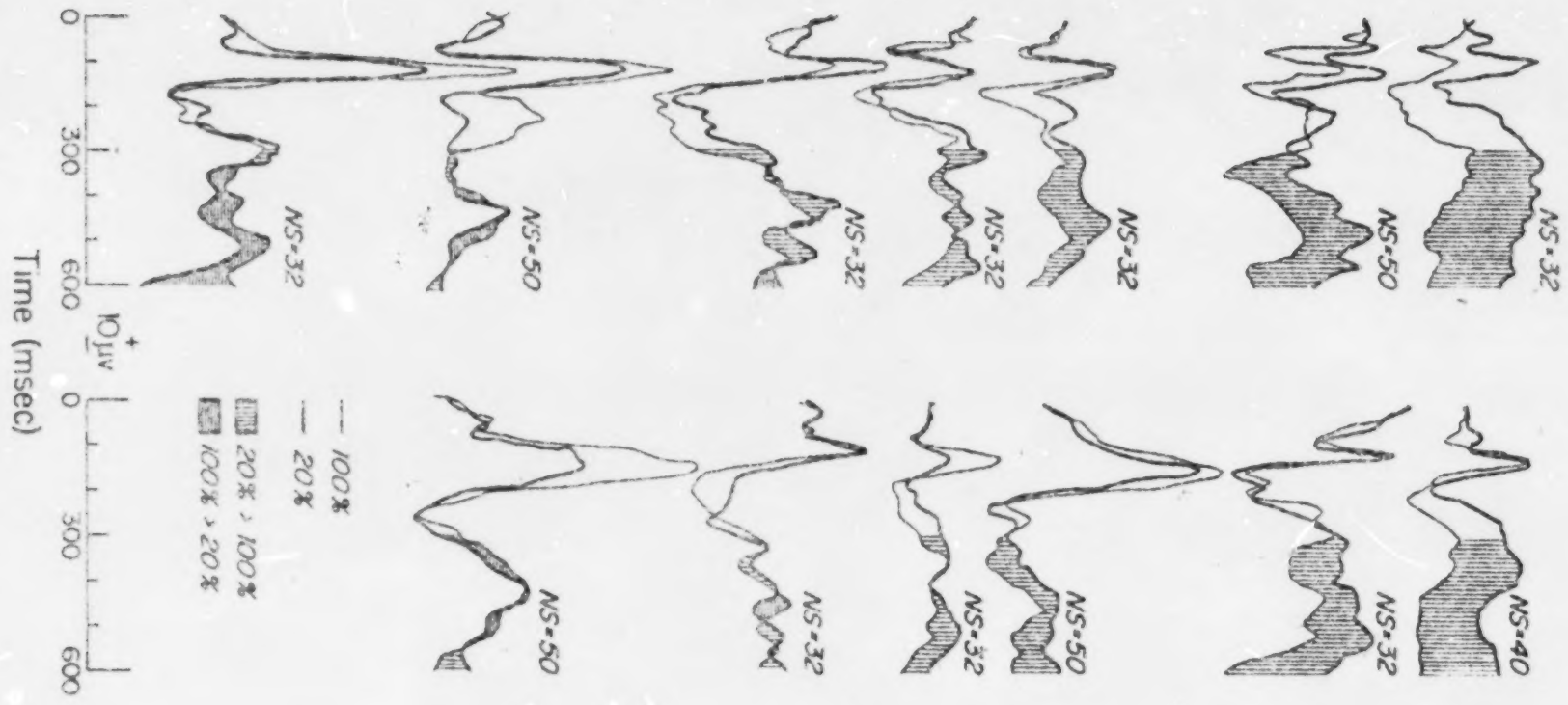


Figure 1. Data from O_z are plotted for the 13 infants. The AEP from the familiarization phases (100%) and the AEP from the low probability trials (20%) are superimposed with respect to initial baseline. The darker trace is the AEP from the low probability trials (20%). Vertical shading indicates greater positive voltage in the 20% AEP relative to the 100% AEP. Horizontal shading indicates greater positive voltage in the 100% AEP relative to the 20% AEP. Area shading extends from 300 msec to 600 msec. NS refers to the number of sweeps (trials) used in the average. Each AEP plot consists of at least 32 trials. For each infant an equal number of trials is included in both the 100% and the 20% traces. Positivity is up.

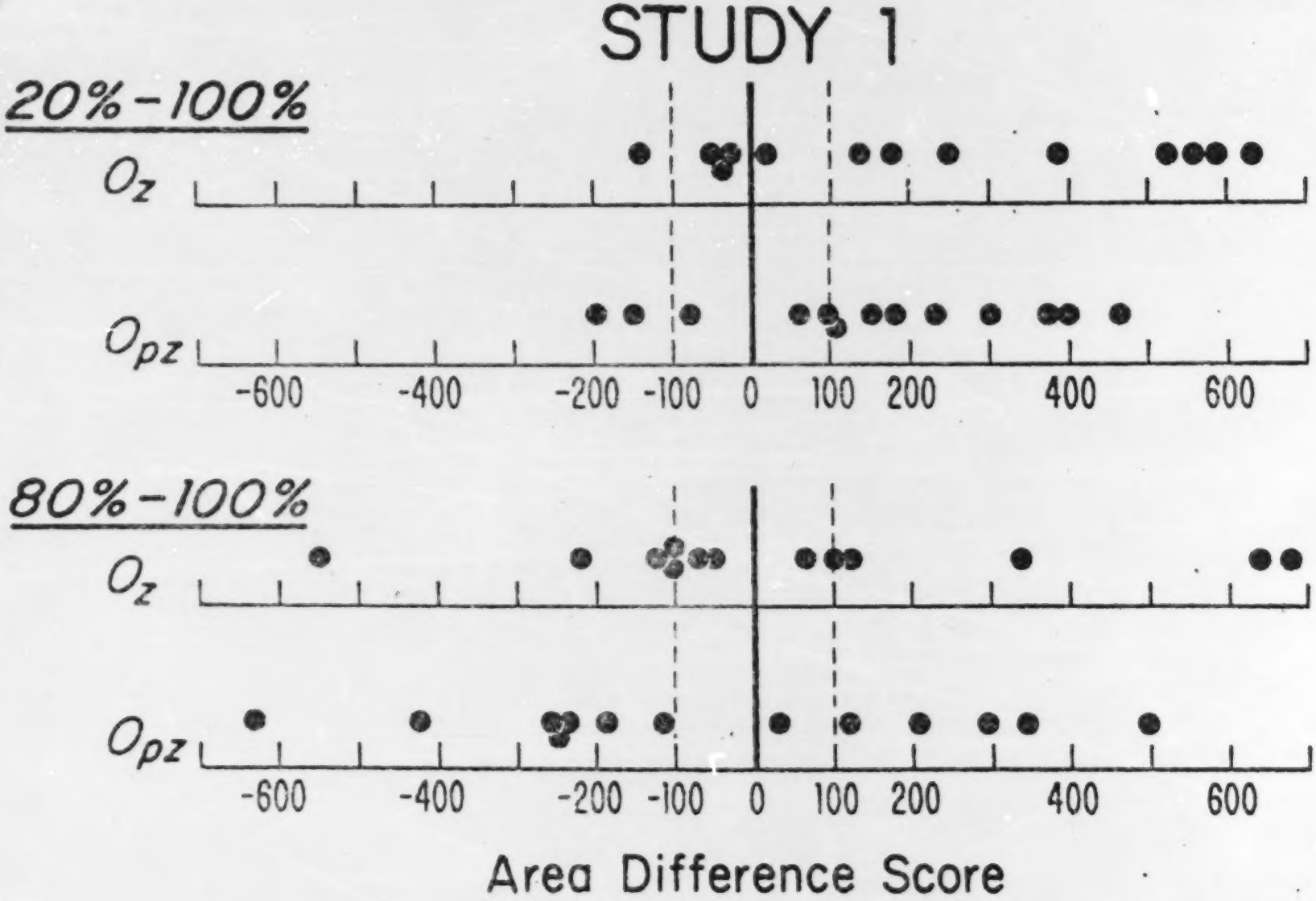


Figure 2. Area difference scores are plotted for each infant in Study 1. The top two plots show the scores obtained from the 20% minus 100% comparisons for Oz and Opz. The bottom two plots provide the scores obtained from the 80% minus 100% comparisons for Oz and Opz.

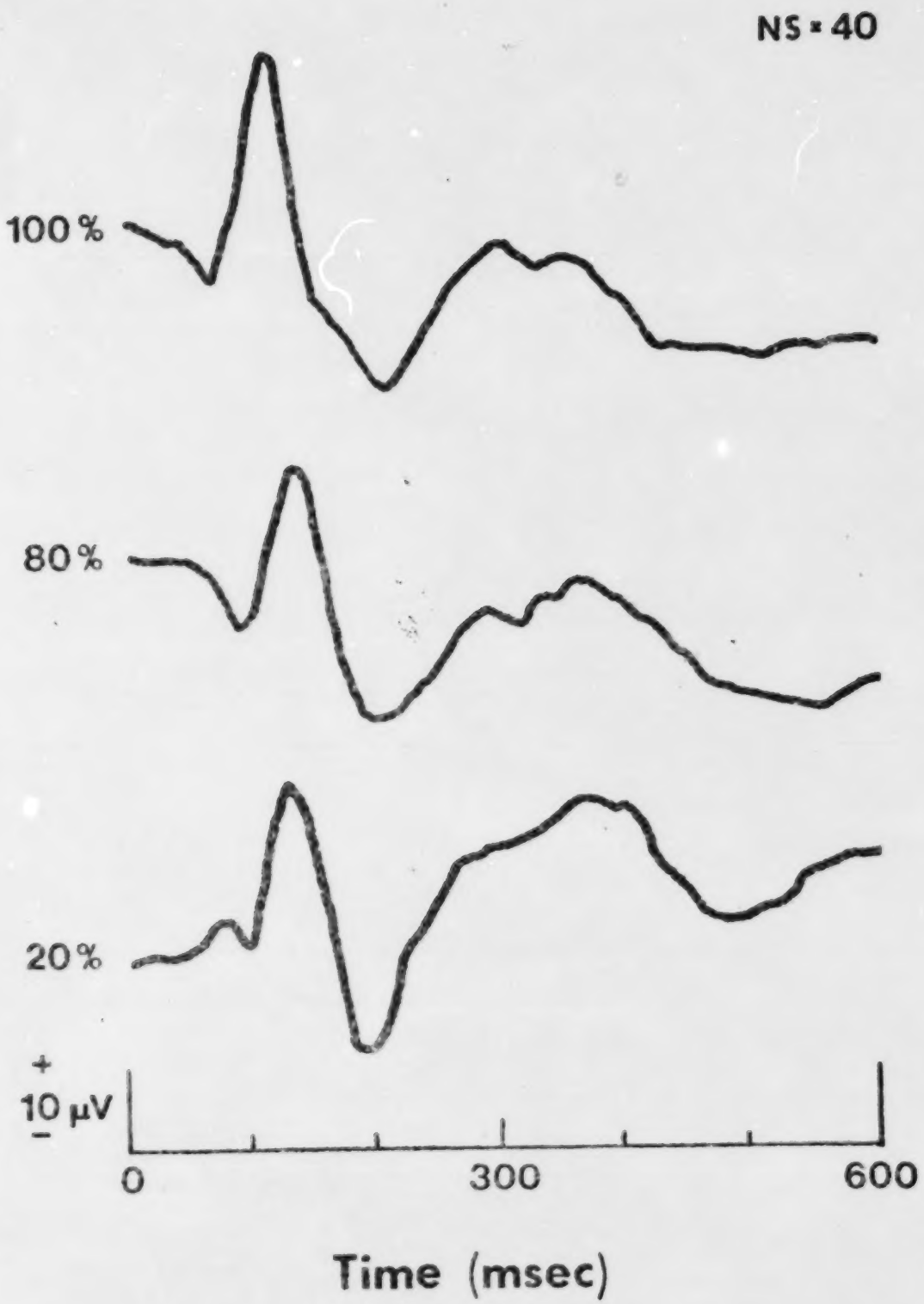
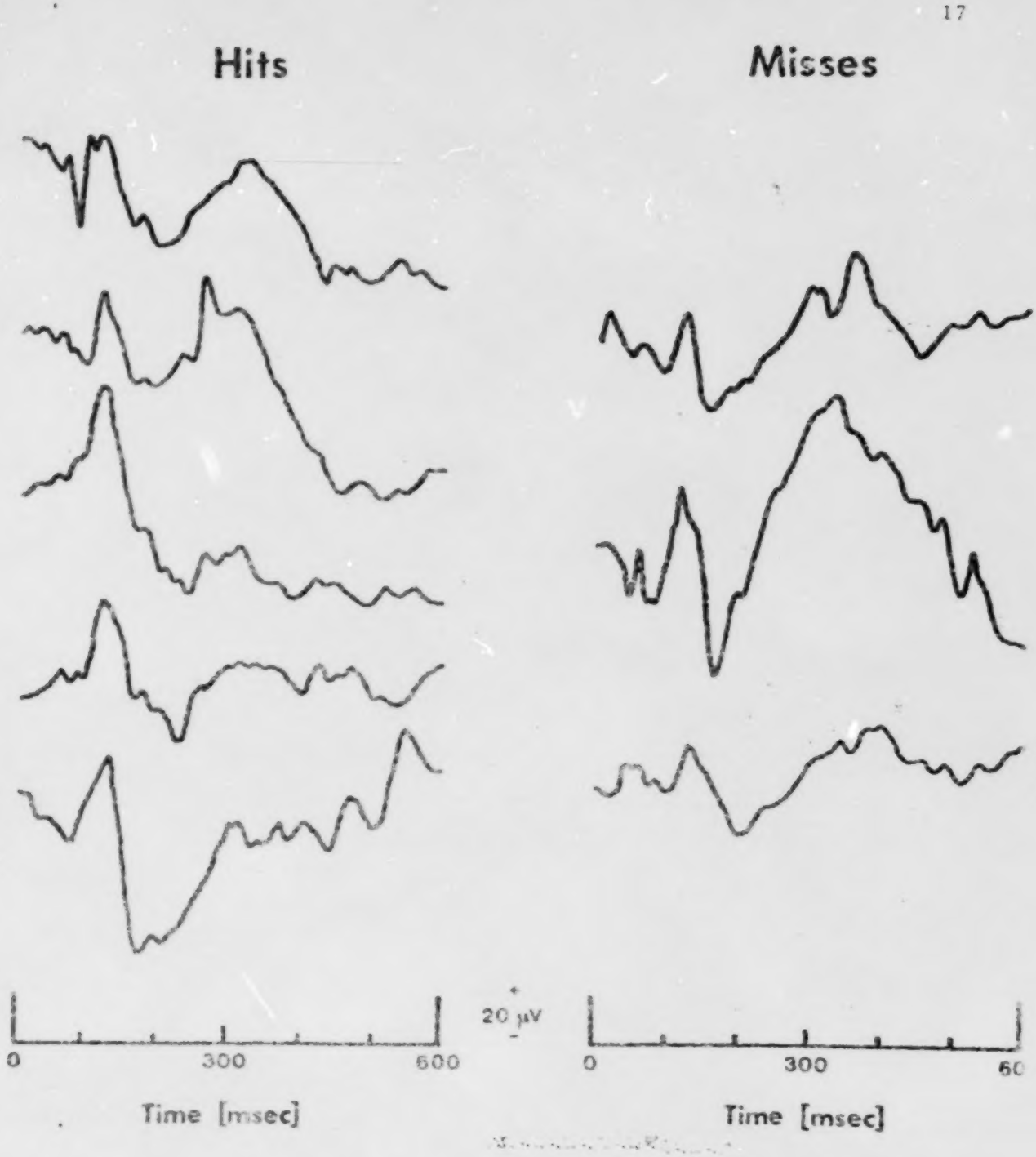


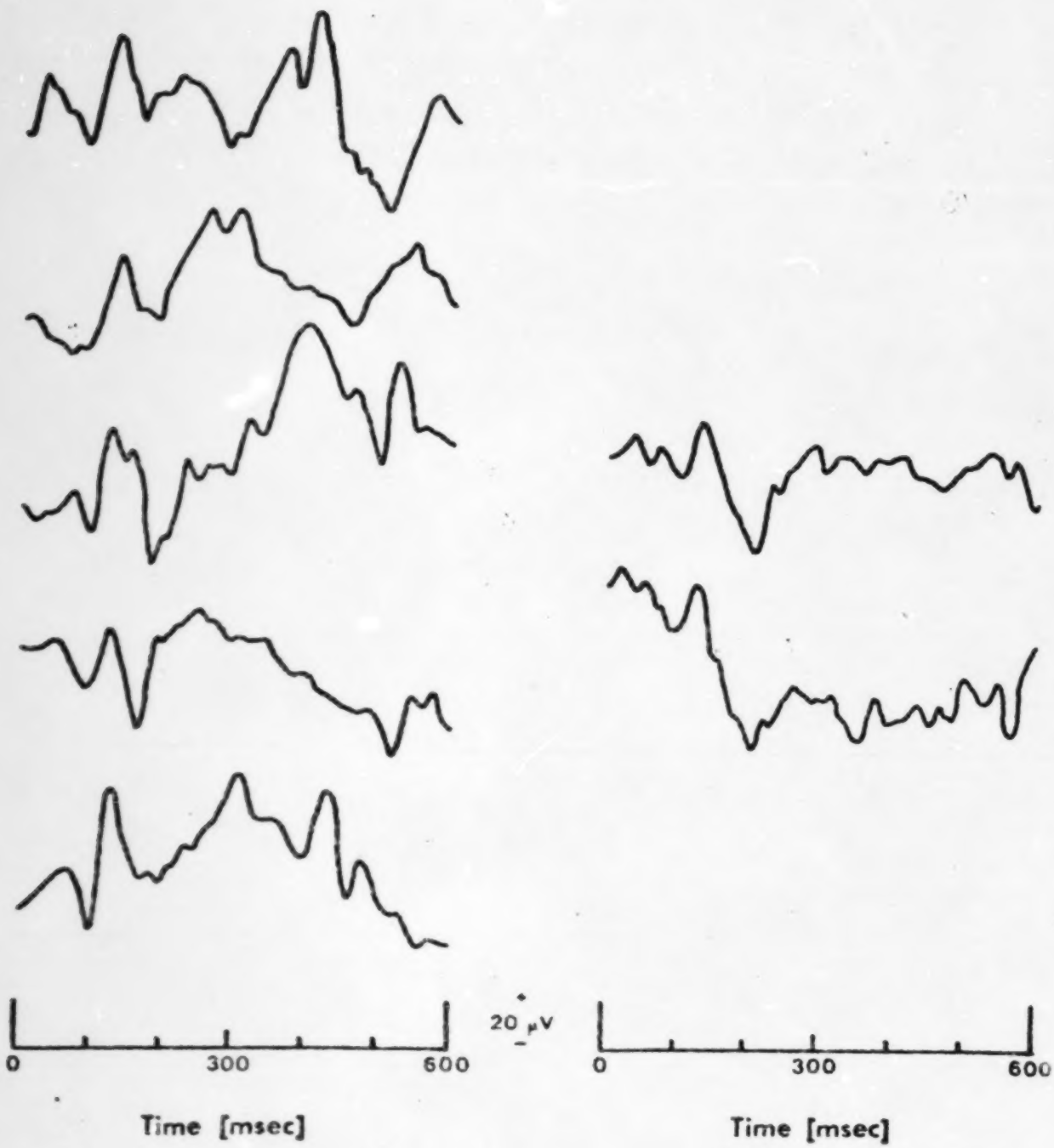
Figure 3. The AEP from the 100%, 80% and 20% conditions for subject J.R. Note that in the 20% condition there is enhancement of the LPC relative to the 100% condition.



Single Trial Evoked Potentials

100% Condition

Figure 4. Examples of single trial EPs from the 100% condition are plotted for subject J.R. Hits are instances of trials correctly identified by the discriminant analysis as 100% trials. Misses are instances of 100% trials that were incorrectly identified as 20% trials.



Single Trial Evoked Potentials
20% Condition

Figure 5. Examples of single trial EPs from the 20% condition are plotted for subject J.R. Hits are instances of trials correctly identified by the discriminant analysis as 20% trials. Misses are instances of 20% trials that were incorrectly identified as 100% trials.

Discriminant Prediction of Single Trials

20% Condition

Trial	Hit	Miss
1		X
2	X	
3		X
4	X	
5		X
6		X
7	X	
8		X
9		X
10	X	
11	X	
12		X
13	X	
14	X	
15	X	
16		X
17	X	
18	X	
19	X	
20	X	
21	X	
22	X	
23	X	
24	X	
25	X	
26	X	
27	X	

Figure 6. Artifact-free single trials from the 20% condition are provided for a subject who did not show a strong LPC effect in the averaged evoked potential analysis. Trials are ordered in the sequence in which they occurred. Trials 1-15 are from the first test phase; trials 16-27 are from the second test phase. Note the pattern of consecutive hits in the second test phase as compared to the first.